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Bloodtyping and Twin Zygosity
Reassessment and Extension

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The determination of twin zygosity by bloodtyping is reconsidered, and the model for the individual case is reformulated. The crucial diagnostic question may be phrased as follows: Given the particular array of bloodgroup phenotypes that the twins display and are concordant for, how might this array have been obtained by a pair of dizygotic twins, and how might the array have been obtained by a monozygotic pair? The solution yields a differential probability value that is uniquely tailored to the actual phenotype array shown. The procedure offers a coherent and more direct method for arriving at the needed probability figures, and it is recommended to supersede previous methods. Some similarities and differences between the methods are discussed.

Key words: Twin zygosity diagnosis, Bloodtyping, Genetic markers

INTRODUCTION

The use of bloodtyping to establish the zygosity of twins has a very active history, beginning with the widely cited papers of Smith and Penrose [2] and Sutton et al [3], and it has recently received another extensive treatment by Lykken [1]. The advantages of bloodtyping are well known and need be only briefly summarized: 1) Bloodtyping furnishes an objective measure of concordance for biological markers that are genetically determined and invariant; and 2) the details concerning gene frequencies, dominant vs recessive alleles, the mechanisms of transmission via different mating combinations, and the expected distribution of phenotypes among offspring are known in sufficient detail to allow a statistical estimate of concordance among twins.

In a prior paper [4] the method for computing the expected number of concordant and discordant dizygotic (DZ) twins in the population was illustrated in detail for each phenotype among the eight major red-cell bloodgroups. The same paper showed a consistent fit between the expected values and the actual distribution of concordant/discordant pairs for each bloodgroup in a large sample of over 300 same-sex DZ pairs. The results were taken as confirming the basic genetic assumptions and methods of calculation for determining the distribution of bloodgroups among two-zygote pairs, which is the critical first step in zygosity analysis.

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The major problem in zygosity diagnosis, however, has been the translation of population statistics into a format appropriate for the individual case, since this is where the crucial diagnostic decisions must be made. The problem derives in part from the unusual nature of the question asked – what is the likelihood of a twin pair being concordant on all major bloodgroups and actually being DZ rather than monozygotic (MZ)? The problem also derives from the complexity of the calculations involved and from some cryptic and recondite formulations of the differential probability estimates that bear on the likelihood of a concordant twin pair being MZ or DZ. These formulations have led to some confusing transitions from probabilities to odds and back again, and in a manner that tends to defeat any understanding of how the requisite values were obtained.

The present article addresses specifically the question of computing the correct probability for each concordant twin pair that the twins may be MZ or DZ. The reader is referred to an earlier article for an extensive detailing of the calculations and results for the entire bloodtyped sample [4]. The final section of that article, however, dealing with prediction for the individual case (p 48 ff), is superseded by the present article.

The original formulation drew on the method of letting the first twin define the reference phenotype, and then setting the probability of concordance as being equal to the likelihood of drawing another single zygote from the capable matings that would display the designated phenotype. As will be shown below, however, this single zygote p-value needs to be supplemented by the p-value for drawing two concordant zygotes in order to obtain the final probability estimate. Therefore, the phenotype values in Table 18 of the 1970 paper are not sufficient by themselves to yield the likelihood of being DZ when concordant, but must be incorporated with the additional two-zygote probabilities to be presented herein. The logic of the procedure will become apparent as the exact nature of the prediction problem is fully defined.[1]

MODEL FOR INDIVIDUAL CASE

In developing the model for the individual case, it becomes imperative to state the exact conditions under which the bloodtyping data will be examined to establish the zygosity of the twins. These conditions may be briefly enumerated.

1) Only same-sex pairs are bloodtyped for zygosity purposes, since opposite-sex pairs are automatically known to be DZ on the basis of the sex difference. Any p-value used to represent the proportion of DZ twins in the bloodtyped sample must be based on the estimated proportion of DZ twins among same-sex pairs.

2) Discordance for any of the bloodtyping tests automatically classifies the pair as DZ, since it demonstrates a genetic difference at one or more loci.

3) The question of differential diagnosis arises only for those pairs that are concordant for all bloodgroups tested. All MZ pairs will be concordant, and a few DZ pairs will also be concordant. The needed figure for each pair is the likelihood that the twins could be DZ rather than MZ.

[1]Incidentally, readers familiar with Lykken's article may recall his allegation of error in my treatment of drawing concordant twins from the capable matings for each phenotype. Lykken's allegation is incorrect and appears to reflect a misunderstanding about how the capable-mating probabilities are computed and used. The calculations are illustrated in full in Appendix 2. As indicated in the text, the original values in the 1970 paper continue to be correct for the single-zygote case, but are now employed with the two-zygote values to be presented later.

4) Although the diagnostic question arises for each concordant pair, no matter what the actual phenotypes are, it is a fact that some phenotypes are much more frequent than others – the O phenotype, for example, in comparison to A_1B. These differences have a significant influence on the likelihood of drawing two concordant zygotes, and therefore the overall probability of being DZ must accurately reflect the p-value for the specific array of phenotypes displayed by the twins.
5) Typically, bloodtyping data are not available for the parents, so the appropriate probabilities must be cast in terms of drawing a pair of concordant twins from all the mating combinations capable of producing the observed phenotypes.

CONCORDANCE ESTIMATES FOR DIZYGOTIC TWINS

As a prologue to the individual case, it will be useful to review the proportion of DZ twins expected to be concordant for each of the major bloodgroups, since these figures are ultimately combined to yield the small number of DZ pairs that will be concordant at all eight loci. The values are shown in Table 1, and they represent the total proportion of concordant DZ twins for all the phenotypes within each bloodgroup [from Wilson: 4].

TABLE 1. Expected Proportion of Concordant DZ Pairs for Each Major Blood Group

Bloodgroup	Proportion concordant
ABO	0.626
Rhesus	0.434
MNSs	0.442
P	0.774
Kell	0.919
Kidd	0.783
Duffy	0.737
Lewis[a]	0.792

It is evident that a substantial number of DZ pairs are expected to be concordant – over 50% for all groups except Rh and MNSs. Since the genes for each bloodgroup segregate independently, the proportion of DZ pairs expected to be concordant across all eight bloodgroups is given by the cumulative multiplication of the eight p-values:

$$\text{Proportion concordant when DZ} = (0.626)(0.434) \ldots (0.792) = 0.039 \quad (1)$$

In a sample composed solely of DZ pairs, the proportion of pairs expected to be concordant at all eight loci is 0.039. When this is considered in terms of the individual pair rather than the sample, the likelihood of any randomly drawn DZ pair being concordant at all loci is also 0.039. Note that this makes no reference to the particular phenotypes being displayed – simply that in a large sample of DZ twins, the expected proportion that will be concordant is 0.039, without restriction as to phenotype.

This value leads in turn to the solution for a mixed sample containing both MZ and DZ pairs. The number of concordant pairs in the mixed sample will include all the MZ pairs, who are by definition concordant at every loci, plus 0.039 of the DZ pairs. Depending on the ratio of MZ twins to DZ same-sex twins in the sample, these values then determine the likelihood that a concordant pair will be DZ.

For example, in the large bloodtyped sample reported previously [4], it was found that 45.8% of the same-sex pairs were DZ, and 54.2% were MZ. Employing these proportions with the figures above, the total proportion of pairs expected to be concordant is given by

$$\begin{aligned}\text{Proportion concordant pairs} &= \text{pDZ (p concordant when DZ)} + \text{pMZ (p concordant when MZ)} \\ &= (0.458)(0.039) + (0.542)(1.000) \\ &= 0.560 \end{aligned} \quad (2)$$

When we consider the concordant pairs in terms of zygosity diagnosis, the expected proportion of concordant pairs that will be DZ is given by

$$\begin{aligned}\text{Proportion DZ among concordant pairs} &= \frac{\text{pDZ (p concordant when DZ)}}{\text{Total proportion concordant pairs}} \\ &= \frac{(0.458)(0.039)}{0.560} \\ &= 0.032 \end{aligned} \quad (3)$$

The corresponding proportion for MZ twins is given by

$$\begin{aligned}\text{Proportion MZ among concordant pairs} &= \frac{\text{pMZ (p concordant when MZ)}}{\text{Total proportion concordant pairs}} \\ &= \frac{(0.542)(1.000)}{0.560} \\ &= 0.968 \end{aligned} \quad (4)$$

Given these values, this means that a pair drawn strictly at random from the concordant pool has a probability of $p = 0.032$ for being DZ. Note again that the phenotypes for the random pair are unspecified -- the probability of 0.032 is an aggregate value representing the average for all possible arrays of concordant phenotypes that the twins might display on a chance basis.

As such, the aggregate value is not exact for any given pair of twins. Furthermore, we are rarely interested in the random-draw case, since the zygosity question must be faced for each concordant pair. But the main significance of this aggregate value is that it defines the central value around which the individual probabilities will be distributed.

CALCULATIONS FOR EACH CONCORDANT PAIR

With these considerations in mind, we turn to the method of calculation for the individual case. The bloodtyping results identify a specific array of phenotypes for which the twins are concordant. Since the eight major bloodgroups segregate independently, the eight phenotypes actually displayed by the twins represent a chance combination of eight independent events. The likelihood of getting this exact array of phenotypes is thus a composite p-value, obtained by cumulatively multiplying the probabilities for the eight phenotypes involved.

The primary question to be asked for each concordant pair is this: Given the specific array of phenotypes displayed by the twins, how might this array have been obtained by a pair of DZ twins, and how might the array have been obtained by a pair of MZ twins? The phrasing of the question is crucial, since the final solution must reflect the differential likelihood of this particular array being obtained by either DZ or MZ twins.

DZ Origin. For DZ twins, it would require drawing two independent zygotes from the capable matings, both of whom were concordant for the first reference phenotype (eg, A_1

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of the ABO bloodgroup). The same requirement would be in effect for each of the remaining bloodgroups and would be expressed as the probability of drawing two independent matching zygotes for each phenotype from the capable matings. Thus, if the likelihood of drawing one zygote of a given phenotype were p = 0.25, the likelihood of drawing two independent matching zygotes would be (0.25)(0.25) = 0.0625. These resultant p-values, appropriately weighted for each mating combination,[2] would then be cumulatively multiplied to yield the composite probability that a DZ pair would display and be concordant for this particular array of phenotypes.

MZ Origin. For MZ twins, it would require drawing one zygote from the capable matings that would display the first reference phenotype (eg, A_1). This zygote, however, has subsequently created an exact replica of itself, so the likelihood of the second twin matching the first on the reference phenotype is 1.00. Thus, the likelihood of an MZ pair displaying the reference phenotype A_1 is given by the probability of drawing a single A_1 zygote from the capable matings, which is then multiplied by 1.00 for concordance in the second twin.

The same requirement would apply for each of the remaining bloodgroups, and would yield a value equal to the probability of drawing one zygote from the capable matings that would display the reference phenotype. Each phenotype value is multiplied by 1.00 for second-twin concordance – a redundancy worth emphasizing here to demonstrate the equivalence with the DZ twin calculations – and the resultant values are then cumulatively multiplied for the eight phenotypes. Thus, the likelihood of an MZ pair displaying and being concordant for this particular array of phenotypes is given by the composite p-value of obtaining a single zygote from the capable matings that would display this exact array.

For each concordant pair in the sample, two p-values are now generated that are uniquely tailored to the particular array of phenotypes displayed by the pair. These are the crucial values needed, and it is important to note that they both incorporate a measure of how probable (or improbable) this particular array of phenotypes would be. Since it is the array actually obtained, the decisive question concerns the relative likelihood of obtaining this array for twins derived from a single zygote versus obtaining the array for twins representing two zygotes.

ILLUSTRATIVE CASES

For example, suppose the bloodtyping data for a particular pair of twins showed them to be concordant on the following phenotypes: O, CDe/cde, Ms/Ns, P+, K–, Jk^a+, Fy^a+, and Le^a–. The likelihood of drawing each phenotype from the capable matings is shown in Table 2 for both conditions.

The composite p-value at the bottom of each column shows that a DZ pair would have a much smaller probability of displaying and being matched for this exact array than would an MZ pair.

These two composite p-values furnish the essential figures needed for the final zygosity equation. The final step in computing the desired probability is to weight each of the above p-values in accordance with the estimated proportion of same-sex DZ and MZ twins in the sample. The proportions may either be inferred from population values or directly estimated from a bloodtyped sample. As indicated earlier, the proportions found in the Louisville Twin Study for 708 same-sex pairs were 45.8% DZ and 54.2% MZ.

[2]The calculations are cumbersome since they require the complete enumeration of all possible mating combinations and all possible pairs of offspring within each bloodgroup. The procedure is illustrated for the P system in Appendix 1, and generalizes to all other systems. The adjustment for the capable matings is given for all phenotypes in Appendix 2.

TABLE 2. Likelihood of Obtaining Reference Phenotypes for Concordant DZ Twins and MZ Twins

Bloodgroup	Reference phenotype	p if DZ twins	p if MZ twins
ABO	O	0.415	0.582
Rhesus	CDe/cde	0.228	0.472
MNSs	Ms/Ns	0.202	0.411
P	P+	0.670	0.791
Kell	K−	0.875	0.916
Kidd	Jk^a+	0.686	0.802
Duffy	Fy^a+	0.574	0.727
Lewis	Le^a−	0.704	0.813
	Composite p =	0.003112	0.038777

Note: Individual p-values represent the likelihood of obtaining each reference phenotype from the capable matings.

These proportions are then employed with the above p-values to compute the final desired probability; namely, that a pair concordant for this specific array of phenotypes would be DZ. The equation is the same as the one previously used with the population values but now modified to be appropriate for the individual case where the phenotype array is fully specified. Thus,

$$\text{pDZ when concordant} = \frac{(\text{pDZ})(\text{p obtaining this concordant array if DZ})}{[(\text{Above}) + (\text{pMZ})(\text{p obtaining this concordant array if MZ})]} \tag{5}$$

Note that the numerator represents the weighted likelihood of drawing a DZ pair concordant on this array, while the denominator represents the total proportion of pairs in the sample expected to be concordant for this array (DZ plus MZ inclusive). The final figure to be computed, then, is the likelihood of the concordant pair being DZ in relation to all concordant pairs for this array.

Substituting the appropriate figures,

$$\text{pDZ when concordant for this array} = \frac{(0.458)(0.003112)}{(0.458)(0.003112) + (0.542)(0.038777)}$$

$$= \frac{0.001425}{0.022442}$$

$$\text{pDZ} \ldots = 0.063 \tag{6}$$

The corresponding likelihood of being MZ is computed by substituting the appropriate MZ values in the numerator:

$$\text{pMZ when concordant for this array} = \frac{(\text{pMZ})(\text{p obtaining this concordant array if MZ})}{[\text{pDZ}(\text{p this array if DZ}) + \text{pMZ}(\text{p this array if MZ})]}$$

$$= \frac{(0.542)(0.038777)}{(0.022442)}$$

$$\text{pMZ} \ldots = 0.937 \tag{7}$$

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TABLE 3. Probability of Obtaining Reference Phenotypes from Capable Matings for Concordant DZ Twins and MZ Twins

System	Phenotype	p if DZ	p if MZ	System	Phenotype	p if DZ	p if MZ
ABO	O	0.415	0.582	MNSs	MS/MS	0.158	0.365
	A_1	0.338	0.548		MS/Ms	0.150	0.353
	A_2	0.202	0.420		Ms/Ms	0.148	0.348
	B	0.217	0.435		MS/NS	0.112	0.311
	A_1B	0.092	0.287		MS/Ns	0.166	0.381
	A_2B	0.077	0.269		Ms/Ns	0.202	0.411
Rhesus	cde/cde	0.191	0.391		NS/NS	0.087	0.280
	CDe/cde	0.228	0.472		NS/Ns	0.132	0.335
	CDe/CDe	0.177	0.395		Ns/Ns	0.191	0.390
	CDe/cDE	0.140	0.356	Kell	K+	0.282	0.523
	cDE/cde	0.152	0.396		K–	0.875	0.916
	cDE/cDE	0.096	0.304	Kidd	Jk^a+	0.686	0.802
	cDe/cde	0.113	0.351		Jk^a–	0.248	0.443
	Cde/cde	0.112	0.411	Duffy	Fy^a+	0.574	0.727
	cdE/cde	0.123	0.791		Fy^a–	0.338	0.520
P	P_1 or P+	0.670	0.791	Lewis	Le^a+	0.236	0.432
	P_2 or P–	0.259	0.453		Le^a–	0.704	0.813

These are the desired probabilities that a twin pair, concordant for this specific array of phenotypes, will be either DZ or MZ. Incidentally, the selected phenotypes were the ones with the highest probability of being concordant if DZ in each blood group, and so the composite p-value represents the maximum likelihood that a concordant pair might be DZ. Other pairs with different arrays will have smaller probabilities of being DZ – ie, $p \leqslant 0.06$.

The procedure outlined above generalizes to every other possible array that might be obtained from twins. The necessary phenotype values may be found in Table 3, which gives both the two-zygote value and the one-zygote value for each individual phenotype.[3] When a concordant pair is examined, the appropriate values are selected from Table 3 for the actual phenotypes observed, and these values are subsequently combined to yield the two needed composite p-values. The latter are then processed through equations (5) and (7), with an adjustment in the MZ/DZ proportions if necessary.

For illustration, two other arrays of phenotypes have been analyzed, one including some medium-frequency phenotypes in ABO, MNSs, and Rh; the other including mainly low-frequency phenotypes, which should yield a much smaller probability that the concordant pair would be DZ. The calculations are summarized in Table 4.

In the first case, the probability of being DZ was $p = 0.045$, and in the second case the probability was much smaller, $pDZ = 0.003$. Clearly, the precision of diagnosis depends upon the particular array of phenotypes displayed by the twins, and it can be shown that the pDZ-values for all possible arrays will fall in the range between 0.002 and 0.063, with a skew towards the average value of 0.032. An investigator can expect that the probability of being DZ for all concordant pairs will fall within this range (assuming MZ/DZ proportions and gene frequencies comparable to the present sample).

This procedure may be employed with fewer than eight blood groups, and it may also be expanded to handle additional systems (eg, serum proteins, red cell enzymes), provided the data are available in appropriate form for inclusion in the phenotype array.

[3]The derivation of the values in Table 3 is described in Appendix 2.

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TABLE 4. Computing the Probability of Being DZ When Concordant for Two Pairs With Different Phenotype Arrays

	"Typical" pair			Pair with low-frequency phenotypes		
Bloodgroup	Reference phenotype	p if DZ	p if MZ	Reference phenotype	p if DZ	p if MZ
ABO	A_1	0.338	0.548	A_1B	0.092	0.287
Rhesus	CDe/CDe	0.177	0.395	Cde/cde	0.112	0.411
MNSs	MS/Ms	0.150	0.353	MS/NS	0.112	0.311
P	P+	0.670	0.791	P–	0.259	0.453
Kell	K–	0.875	0.916	K+	0.282	0.523
Kidd	Jk^a+	0.686	0.802	Jk^a–	0.248	0.443
Duffy	Fy^a+	0.574	0.727	Fy^a–	0.338	0.520
Lewis	Le^a–	0.704	0.813	Le^a–	0.704	0.813
	Composite p =	0.001459	0.026243	Composite p =	0.000005	0.001628

pDZ if concordant this array $= \dfrac{(0.458)(0.001459)}{[(\text{above}) + (0.542)(0.026243)]} = \dfrac{0.000668}{0.014892}$

pDZ ... = 0.045

pMZ if concordant this array $= \dfrac{(0.542)(0.026243)}{0.014892}$

pMZ ... = 0.955

pDZ if concordant this array $= \dfrac{(0.458)(0.000005)}{[(\text{above}) + (0.542)(0.001628)]} = \dfrac{0.0000023}{0.0008847}$

pDZ ... = 0.003

pMZ if concordant this array $= \dfrac{(0.542)(0.001628)}{0.0008847}$

pMZ ... = 0.997

The procedure translates immediately into the case where the parental genotypes are known (the capable matings are simply replaced by the single known mating), and it deals exclusively with probabilities and proportions in computing the needed figure for each phenotype array rather than switching back and forth between probabilities and odds.

Equally important, it preserves the focus on the likelihood that the twins would both display and be concordant for this particular array, first on the hypothesis of DZ origin, then on that of MZ origin. On this basis, the procedure outlined herein is recommended as a simpler, more direct, and more comprehensible method for evaluating bloodtyping data from twins than prior methods.

COMPARISON WITH OTHER METHODS

Any researcher who is not a quantitative geneticist and who has attempted to digest the prior articles in this area will find him/herself struggling with a complicated and technically forbidding mass of material. Perhaps it might be useful to identify the common themes among the various approaches and how they coordinate with one another. As it turns out, there are translation equations that tie the methods together, although the definitions, interpretations, and methods of calculation vary widely.

Smith and Penrose [1955]. This classic paper is, unfortunately, both cryptic and inaccessible in terms of the basic logic and methods of calculation for DZ likelihood. Smith and Penrose originated the procedure of converting probability to odds, as follows: "In England, the basic probability ratio that twins are dizygotic is 70:30 or 2.33:1. These ratios represent the odds in favour of the dizygotic contingency. We can call this the initial relative probability in favour of a dizygotic pair, p_0D. These odds are modified as soon as information about any specific character in a given twin pair is ascertained" [2: p 273].

They then describe how information from bloodtyping data is incorporated into the calculation of odds, or relative probability, for each phenotype. The resultant odds figure may then be multiplicatively combined for any number of independent traits (eg, bloodgroups), leading to a total odds favoring the DZ contingency, pD. The latter is ultimately employed in the formula pD/(1 + pD) to convert back to a true probability that the concordant pair would be DZ.

Smith and Penrose then provide detailed tables of random mating probabilities, parent-offspring frequencies, and the distribution of two-zygote (sib-sib) pairings for a two-allele system (pp 275–276). The diagonal cells of their Table 5 represent the concordant pairs for each phenotype in the system; the off-diagonals represent the discordant pairs, and the marginal totals represent the proportion of pairs for the entire sample in which one or both members display the phenotype in question. They remark, "The relative chance in favour of a dizygotic pair when twins have the same blood group is ... obtained by dividing the number of children in the [diagonal] AA,AA cell, for example, by the total number of AA children" (p 276).

It will perhaps not be evident how the method quoted in the preceding sentence qualifies as an appropriate way to compute the DZ odds. Smith and Penrose give no further explanation, but proceed abruptly into very detailed tables of genotype/phenotype frequencies and sib-sib pairings for all major bloodgroups. Finally they return to two illustrations on pp 286–287, in which the relative chances or odds (computed as described above) are shown, along with the final conversion to the absolute probability of obtaining a DZ pair, pD/(1 + pD).

It is worth emphasizing that Smith and Penrose work from tables of sib-sib pairings in arriving at the DZ contingency figures, and although their description speaks of children rather than pairs, it is a fact that the proportion of children in the AA,AA cell is equal to the proportion of two-zygote pairs concordant for the AA phenotype. Similarly, the total proportion of children displaying the AA phenotype is equal to the one-zygote phenotype frequency in the population; and from the standpoint of pairs, it is also equal to the proportion of two-zygote pairs in which the first member of the pair (as randomly designated) displays the AA phenotype. The latter thus includes all concordant pairs plus one-half of the discordant pairs for AA, as shown in the marginal totals of the Smith and Penrose tables. This particular definition later reappears in the index-case approach of Sutton et al [3] and Lykken [1].

For each phenotype, then, the DZ odds computed by Smith and Penrose may also be obtained by dividing the proportion of concordant two-zygote pairs by the one-zygote phenotype frequency: pD = (p two concordant zygotes)/(p one zygote). The resultant quotient for each phenotype expresses the relative likelihood of obtaining a concordant DZ pair in relation to the one-zygote reference value, where the latter has effectively been set equal to 1.00 by the calculation.

It may be recognized that the above terms (p two concordant zygotes and p one zygote) correspond to the listed entries for each phenotype in Table 3 of the present paper, where they are designated as the "p if DZ twins" and "p if MZ twins," respectively. In fact, Table 3 was constructed from the detailed tables in Wilson [4], showing the expected proportions of single zygotes and concordant two-zygote pairs for all phenotypes.

The further step of division was not made separately for each phenotype, however, since the logic remains much clearer and more straightforward in dealing with the full phenotype array for each twin, first as it might be obtained on the hypothesis of DZ origin, then on that of MZ origin. Indeed, some of the most refractory problems in bloodtyping analysis have arisen from anomalous interpretations of this quotient and what it represents in terms of DZ concordance. In the present approach, the division is accomplished ultimately in the final predictor equation, which deals with the aggregate probability of being DZ if same-sex and concordant for this particular array of phenotypes; and it makes superfluous the intermediate conversion from probabilities to odds and back to probabilities again.

For illustration purposes, however, the values of (p two concordant zygotes)/(p one zygote) have been computed for all phenotypes in the present study,[4] making use of the listed entries in Table 3. These values are presented in the first column of Table 5, and for comparison the corresponding figures from the Smith and Penrose paper are listed in the second column. Given the differences in samples, there is surprisingly high congruence between the two sets of figures.

Sutton, Clark, and Schull [1955]. These authors proceeded by a somewhat different route to obtain the necessary figures for computing the probability of a twin pair being MZ (or DZ) if concordant. Their ultimate predictor equation for MZ likelihood (#4 on p 181) corresponds to equations (4) and (7) of the present paper; and although they do not actually give a formal equation for the DZ likelihood, it is easily obtained and can be shown to correspond to equations (3) and (6) herein. For each zygosity group, their single equation differentiates into the two equations of the present paper, depending on whether a random pair or a particular pair with a designated phenotype array is being considered. Sutton et al also remained in probability format throughout; there was no mention of conversion to odds.

The distinctive feature of their approach was the set of formulas that they devised to obtain the likelihood of DZ concordance for each phenotype in the various bloodgroups. Initially, however, Sutton et al presented a single basic equation for estimating DZ concordance from bloodtyping data, as described below.

When there is no knowledge about parental genotypes and therefore all possible capable matings must be considered, the "probability of a dizygous twin of an offspring of phenotype ϕ_T also being of phenotype ϕ_T" (p 182) is given by their equation 9:

$$P(\phi_T|\phi_T) = \frac{\sum_{j=1}^{n} [P(m_j)[P(\phi_T \mid m_j)]^2]}{\sum_{j=1}^{n} [P(m_j)P(\phi_T \mid m_j)]}$$

[4]Since the capable mating p-value enters into both the two-zygote and one-zygote probabilities, it cancels out in the division, and consequently the same resultant figure is obtained for each phenotype whether using the population frequencies or the mating-adjusted p-values.

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TABLE 5. Relative Likelihood of Two-Zygote Origin for Concordant Twins, as Computed in Three Studies

Phenotype	Wilson	Smith & Penrose	Lykken/ Sutton et al	Phenotype	Wilson	Smith & Penrose	Lykken/ Sutton et al
O	0.713	0.689	0.675	MS/MS	0.433	0.389	0.381
A_1	0.617	0.647	0.639	MS/Ms	0.426	0.418	0.425
A_2	0.479	0.482	0.477	Ms/Ms	0.425	0.412	0.425
B	0.499	0.474	0.487	MS/NS	0.359	0.342	0.336
A_1B	0.320	0.324	0.330	MS/Ns	0.435	0.456	0.428
A_2B	0.286	0.285	0.290	Ms/Ns	0.490	0.473	0.482
cde/cde	0.488	0.482	0.486	NS/NS	0.309	0.292	0.288
CDe/cde	0.483	0.540	0.540	NS/Ns	0.393	0.383	0.376
CDe/CDe	0.448	0.502	0.509	Ns/Ns	0.489	0.483	0.472
CDe/cDE	0.394	0.424	0.424	K+	0.539	0.545	0.540
cDE/cde	0.384	0.418	0.418	K−	0.956	0.948	0.955
cDE/cDE	0.315	0.332	0.341	Jk^a+	0.856	0.853	a
cDe/cde	0.324	0.368	0.357	Jk^a−	0.560	0.568	0.573
Cde/cde	0.269	0.351	0.350	Fy^a+	0.789	0.804	a
cdE/cde	0.139	0.352	0.349	Fy^a−	0.651	0.632	0.600
P+	0.847	0.849	0.875	Le^a+	0.547	0.542	0.575
P−	0.573	0.570	0.533	Le^a−	0.865	0.868	a

[a]Lykken does not give this value in a form comparable to the other two authors.

where $P(m_j)$ is the probability, based solely on gene frequencies, of parental mating combination m_j, and $P(\phi_T | m_j)$ is the probability of obtaining from mating combination m_j an offspring of phenotype ϕ_T. When the above probability is computed for each concordant phenotype, the final aggregate probability is obtained by multiplying together the f independent probabilities involved.

In examining their equation 9, it becomes evident that the numerator represents the weighted probability of drawing two concordant zygotes for a particular phenotype from the capable matings, while the denominator represents the probability of drawing a single zygote. It thus becomes an identity with the previously described computation of Smith and Penrose, ie, (p two concordant zygotes)/(p one zygote), and to the equivalent computation in the present paper, as illustrated in Table 5. The three approaches are therefore linked through this one common relationship.

While Sutton et al [3] mention that their equation 9 is general in the sense of applying to multiallele systems, various dominance relationships, etc, and can always be employed to compute the needed $P(\phi_T | \phi_T)$, by far the largest part of their paper is devoted to alternative methods of computing this value for various phenotypes. It is perhaps unfortunate that the alternative methods comprise a variety of equations that employ only gene frequencies for their solution, and consequently the resultant answers seem detached and remote from the original terms entering into equation 9.

Lykken [1: p 439] describes the equations as "simple and elegant formulas for computing the probabilities of DZ concordance on Mendelizing traits;" but it is worth noting that, as represented in equation 9, the so-called probability of DZ concordance is not the same as the two-zygote concordance value, which is shown in the numerator. Rather, it is the relative likelihood of two-zygote concordance in relation to the one-zygote value (or the latter's equivalent, the proportion of two-zygote pairs in which the random prospectus displays the reference phenotype).

When this latter definition is employed, the probability of DZ concordance then becomes narrowly defined in terms of the index-case approach: If the sample is restricted solely to those pairs in which the randomly chosen prospectus twin displays the reference phenotype, and the prospectus is taken as the index case, what is the likelihood that the cotwin will match the prospectus for the reference phenotype? The resultant figure is neither the probability of drawing two concordant zygotes nor the probability of drawing a single independent zygote with a matching phenotype, but rather the ratio of the two. The distinction is sometimes blurred, however, as in Lykken's description of DZ concordance: "... one can compute the aggregate probability (and hence the odds) that the parents who could have produced twin A (arbitrarily taken as the prospectus) might independently produce another offspring with the same phenotype (such as a DZ cotwin of twin A)" [1: p 445; parentheses in original].

Lykken [1978]. Lykken merged features from both of the preceding papers in his analysis of twin zygosity. He adopted the DZ odds approach of Smith and Penrose to compute the initial and final probability figures, but he employed the equations of Sutton et al to obtain the likelihood of concordance for DZ twins on each phenotype. Since the Sutton et al equations generate probabilities according to their definition, Lykken then divided the DZ p-value for each phenotype by 1.00, which he justified as representing the probability of concordance for MZ twins. Consequently, the entire set of probability values derived from the Sutton et al equations were converted into an exactly equivalent set of values called DZ odds.

Before appraising Lykken's method, it will be instructive to compare the DZ concordance values he obtained, since they furnish actual results from the Sutton et al equations, which had not been previously furnished by the authors. Lykken's bloodtyping data were drawn mainly from Minnesota whites of European origin, and the computed values are shown in the third column of Table 5 of the present paper (from Lykken [1]: Tables 6, 7, 8, and 9).

Inspection of Table 5 shows a high degree of similarity between all three sets of values – and this in the face of three different populations from which the underlying gene frequencies were determined. Apparently the minor variations in gene frequencies among these white populations had only a limited effect on the computed concordance values for DZ twins. It is also evident that all three procedures can be made equivalent through this one computation of (p two concordant zygotes)/(p one zygote) for each phenotype.

Returning to the interpretation of the computed values, Smith and Penrose treated these figures as DZ odds, without the further stratagem of dividing by 1.00, while Sutton et al treated them as probabilities throughout. Lykken, however, computed by the latter procedure but then redefined the same value in terms of the former DZ odds approach. One advantage of dividing by 1.00, of course, is that nothing changes, and consequently Lykken gets to the same final probability figure as the other approaches. But the transition back and forth from odds to probabilities provides ample room for conceptual slippage and ambiguity, and this has been perhaps the most difficult problem in clarifying the model for the individual case since the original paper of Smith and Penrose.

Another difficulty lies in the very sketchy detailing of what the DZ figure as computed for each phenotype actually represents. As indicated earlier, it is something of a misnomer to call it the probability of DZ concordance, and perhaps another interpretation might be offered.

When the two terms of the basic ratio are defined as in the present paper – ie, (p if DZ twins)/(p if MZ twins) – then the resultant figure expresses how closely the likelihood of DZ origin for this concordant pair approaches the likelihood of MZ origin. In the limiting case as this figure approaches 1.00, it means that virtually all two-zygote pairs are concordant for the phenotype, just as the MZ pairs are. Consequently, the fact of concordance provides no differential basis for making a zygosity decision. The Lutheran bloodgroup is a good case in point – practically all two-zygote pairs are concordant – and K- from the Kell bloodgroup is nearly as extreme, with a computed value of 0.956. Neither is useful for zygosity diagnosis.

By contrast, the discrimination power improves as this value declines, since it reflects a smaller likelihood of drawing two independent zygotes that would match on the phenotype in question. The A_2B phenotype is a good example, with a computed value of 0.286; a concordant pair is much less likely to represent two independent zygotes than a single zygote that replicated itself.

From this perspective, it might be suggested that the computed values of Lykken/Sutton et al, and Smith and Penrose, be thought of as DZ plausibility quotients. The larger the value, the more plausible it is that a concordant pair might be DZ in origin, until at the limit of 1.00 the DZ hypothesis is as plausible as the MZ hypothesis.

But as the value declines, the plausibility of DZ origin also declines, and consequently the marker phenotypes become increasingly effective for establishing zygosity. In fact, these values qualify as the efficiency measures for the phenotypes; the smaller the value, the more efficient the phenotype in discriminating between MZ and DZ pairs. This measure of efficiency, incidentally, is more precise than the efficiency index of Lykken/Sutton et al, which depends only on the expected proportion of concordant two-zygote pairs.

By way of final coordination among methods, it may be noted that the predictor equation in the present paper for DZ probability (Eq 5) may be made equal to the Smith and Penrose absolute DZ probability equation by dividing each term in equation (5) by the last complete term in the denominator. Similarly, the predictor equation for MZ probability (Eq 7) may be made equal to the Smith and Penrose MZ equation by dividing each term in equation (7) by the last complete term in the denominator. The same conversion holds for the Lykken equations. For Sutton et al, their equation for MZ probability may be obtained from the present MZ equation (Eq 7) by dividing the aggregate value of "p obtaining this concordant array if MZ" into each term of equation (7). They do not give a formal DZ probability equation as such.

FINAL COMMENT

Few areas represent as much of a challenge to comprehension for the nongeneticist as the twin bloodtyping model for the individual case. The present analysis shows that, if correctly employed, the various procedures will all ultimately yield the same probability of being DZ or MZ for a given concordant pair. There are some significant differences in logic and application, however, and the method outlined in this paper is recommended as the simplest and most direct for obtaining the desired probabilities. Readers are invited to consult the other papers to make their own comparison.

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APPENDIX 1

The basic method of computing the probability of concordance for DZ twins may be illustrated for one bloodgroup, since the method generalizes to all other bloodgroups, whether two-allele or multiallele systems.

For illustration, the P bloodgroup is used – it is a two-allele system with P_1 (or P+) dominant.[5] The phenotype P_1 is therefore obtained for the homozygous genotype $p_1{:}p_1$ and the heterozygous genotype $p_1{:}p_2$ (or $p_2{:}p_1$), whereas the phenotype P_2 is obtained only for the homozygous genotype $p_2{:}p_2$.

Drawing from the previous report [4], the gene frequency in the twin population for p_1 was 0.486, and the gene frequency for p_2 was 0.514. Each individual in the population carries one of the three possible genotype combinations of p_1 and p_2, and the expected proportion of each genotype combination is given by the product of the gene frequencies involved:

$$\begin{aligned} &p_1{:}p_1 \ (0.486)(0.486) && = 0.2362 \\ &\left.\begin{array}{l} p_1{:}p_2 \ (0.486)(0.514) \\ \text{or} \\ p_2{:}p_1 \ (0.514)(0.486) \end{array}\right\} && = 0.4996 \\ &p_2{:}p_2 \ (0.514)(0.514) && = \underline{0.2642} \\ & && \quad 1.0000 \end{aligned}$$

In terms of phenotypes, the expected proportion of P_1 phenotypes in the population is given by 0.2362 plus 0.4996 = 0.7358, whereas the proportion of P_2 phenotypes is 0.2642.

When parental mating combinations are formed, the genotype combinations for mother and father reflect the expected distribution that would arise from random mating. Thus a table of all possible mating combinations is generated, and the likelihood of each combination is given by the joint probability of the two genotypes involved. For example, if the mother were $p_1{:}p_1$, and the father $p_1{:}p_2$ (or $p_2{:}p_1$), then the likelihood of this mating combination occurring in the population is given by $(p_1{:}p_1)(p_1{:}p_2 \text{ or } p_2{:}p_1) = (0.2362)(0.4996) = 0.1180$. The probabilities for all possible genotype mating combination within the P system are later shown in Table A-1..

The offspring from each mating combination will reflect the possible sets of genes that may be obtained from the parents. There are four possible outcomes: a) the allele in locus 1 for the father combines with the allele in locus 1 for the mother; b) locus 1 father with locus 2 mother; c) locus 2 father with locus 1 mother; and d) locus 2 father with locus 2 mother.

When this is completely enumerated for all mating combinations, it specifies the possible genotypes for the offspring of each mating and the proportion of offspring expected to possess each genotype. For example, in the first cell of Table A-1, with both parents having p_1 at both loci, the four combinations of alleles will all yield $p_1{:}p_1$ for all offspring, so the proportion of offspring with $p_1{:}p_1$ genotypes will be 1.00.

[5]For clarity, the phenotype of each zygote is designated by a single capital letter, and the two-allele genotype is designated by two lowercase letters.

TABLE A-1. Genotype Mating Probabilities and Proportion of Offspring Showing Reference Phenotype from Each Mating Combination

	Mother genotype		
Father genotype	p_1:p_1	p_1:p_2 or p_2:p_1	p_2:p_2
p_1:p_1	a $P_1 = 1.00$ (0.0558)	b $P_1 = 1.00$ (0.1180)	c $P_1 = 1.00$ (0.0624)
p_1:p_2 or p_2:p_1	d $P_1 = 1.00$ (0.1180)	e $P_1 = 0.75$ $P_2 = 0.25$ (0.2496)	f $P_1 = 0.50$ $P_2 = 0.50$ (0.1320)
p_2:p_2	g $P_1 = 1.00$ (0.0624)	h $P_1 = 0.50$ $P_2 = 0.50$ (0.1320)	k $P_2 = 1.00$ (0.0698)

By contrast, the parents for cell e each have p_1:p_2 genotypes, and the four combinations of alleles would give p_1:p_1 offspring 25% of the time, p_1:p_2 offspring 50% of the time, and p_2:p_2 offspring 25% of the time. The last genotype would yield a P_2 phenotype, whereas the prior combinations would all yield offspring with P_1 phenotypes, so the expected proportion of P_1 offspring would be 0.75 from this mating combination.

The offspring possibilities from each mating combination are summarized in Table A-1, where the offspring phenotypes are given, along with the proportion expected to show the phenotypes. The mating probability for each combination is also included.

The expected proportion of P_1 offspring from all matings is given by the cumulative product of each mating probability times the proportion of P_1 offspring expected from that mating. For cells a through h, respectively, this would yield (0.0558)(1.00) + (0.1180)(1.00) . . . + (0.1320)(0.50) = 0.7358, which corresponds to the proportion of P_1 phenotypes in the population.

Similarly, the cumulative product of the mating probabilities times the proportion of P_2 offspring in cells e, f, h, and k gives the proportion of P_2 phenotypes in the population: (0.2496)(0.25) + (0.1320)(0.50) + (0.1320)(0.50) + (0.0698)(1.00) = 0.2642.

Since for DZ twins the desired information deals with pairs of zygotes from each mating combination, the next step is to enumerate the possible pairings of phenotypes and the likelihood of obtaining each pairing. Each zygote represents an independent and random draw from the possible phenotypes that the parents can produce, so the expected probability for the pair is the joint product of the probabilities for the two phenotypes involved.

This may be computed from the preceding table by pairing the possible phenotypes in each cell and computing the probability for each pairing. In cell a, for example, all offspring will be P_1, so the likelihood of drawing two zygotes with the P_1 phenotype is (1.00)(1.00) = 1.00. By contrast, in cell e the likelihood of drawing two P_1 zygotes is (0.75)(0.75) = 0.5625, while the likelihood of drawing a P_1 zygote and a P_2 zygote is 2(0.75)(0.25) = 0.3750, and the likelihood of drawing two P_2 zygotes is (0.25)(0.25) = 0.0625.

The probabilities for the pairs of zygotes available from each mating combination are summarized in Table A-2.

The final step in computing the expected number of DZ pairs that will show each combination of phenotypes is to multiply the mating probability in each cell times the proportion of pairs from that mating that will display the desired phenotypes, and then sum across all cells. In effect, this combines Table A-2 with the mating probability table, and the results are summarized in Table A-3, below.

TABLE A-2. Probabilities of Two Zygotes Displaying the Reference Phenotypes for Each Mating Combination

Father genotype	Mother genotype $p_1{:}p_1$	Mother genotype $p_1{:}p_2$ or $p_2{:}p_1$	Mother genotype $p_2{:}p_2$
$p_1{:}p_1$	a P_1 and P_1 = 1.00	b P_1 and P_1 = 1.00	c P_1 and P_1 = 1.00
$p_1{:}p_2$ or $p_2{:}p_1$	d P_1 and P_1 = 1.00	e P_1 and P_1 = 0.5625 P_1 and P_2 = 0.3750 P_2 and P_2 = 0.0625	f P_1 and P_1 = 0.25 P_1 and P_2 = 0.50 P_2 and P_2 = 0.25
$p_2{:}p_2$	g P_1 and P_1 = 1.00	h P_1 and P_1 = 0.25 P_1 and P_2 = 0.50 P_2 and P_2 = 0.25	k P_2 and P_2 = 1.00

TABLE A-3. Phenotype Combinations and Associated Probabilities for Pairs of Zygotes in P Bloodgroup

P_1 and P_1			P_1 and P_2			P_2 and P_2		
Cell	Mating probability	Likelihood of P_1 and P_1	Cell	Mating probability	Likelihood of P_1 and P_2	Cell	Mating probability	Likelihood of P_2 and P_2
a	0.0558 ×	1.0000	e	0.2496 ×	0.3750	e	0.2496 ×	0.0625
b	0.1180 ×	1.0000	f	0.1320 ×	0.5000	f	0.1320 ×	0.2500
c	0.0624 ×	1.0000	h	0.1320 ×	0.0500	h	0.1320 ×	0.2500
d	0.1180 ×	1.0000		Composite p =	0.2256	k	0.0698 ×	1.0000
e	0.2496 ×	0.5625					Composite p =	0.1514
f	0.1320 ×	0.2500						
g	0.0624 ×	1.0000						
h	0.1320 ×	0.2500						
	Composite p =	0.6230						
Therefore, proportion of two-zygote pairs, both P_1 = 0.6230			Proportion of two-zygote pairs, P_1 and P_2 = 0.2256			Proportion of two-zygote pairs, both P_2 = 0.1514		

So in a large sample of DZ twins, the expectation is that the bloodtyping results for the P system will conform to the above values: about 0.6230 of the pairs will be concordant for P_1, about 0.1514 of the pairs will be concordant for P_2, and the remainder of the pairs (0.2256) will be discordant, displaying P_1 and P_2. When these values were compared with the actual distribution of DZ pairs, the fit was found to be very close indeed [4: p 39]. Thus, the basic derivations and calculations were confirmed by an empirical test; and this was also true when extended to the other seven bloodgroups.

APPENDIX 2

When a twin pair is found to be concordant on a particular phenotype, it immediately limits the parental mating combinations to those actually capable of producing the phenotype in question. For example, if the twins are concordant on P_2, the possible matings that could be involved are those capable of producing P_2 offspring. The previous tables show that the capable matings for P_2 are associated with cells e, f, h, and k.

These mating combinations now become the complete population of matings from which P_2 offspring may be drawn. Therefore, the likelihood of each capable mating combination is no longer its value in the full table of matings, but rather is adjusted to represent its likelihood among the limited set of P_2-capable matings. This is accomplished by setting the proportion of P_2-capable matings equal to 1.00; then each mating within this limited group is proportionally increased to yield the total of 1.00.

For example, the P_2-capable matings involved for cells e, f, h, and k are shown below in terms of the original mating probabilities and the adjusted probabilities.

Cell	Population mating p-value	Adjusted mating p-value		Likelihood of P_2 and P_2 pair (DZ)	Joint probability of drawing concordant P_2 pair (DZ) from capable matings
e	0.2496	0.4278	×	0.0625	0.0267
f	0.1320	0.2263	×	0.2500	0.0566
h	0.1320	0.2263	×	0.2500	0.0566
k	0.0698	0.1196	×	1.00	0.1196
	0.5834	1.0000			0.2595

Given the possible matings that can produce P_2 zygotes and the expected offspring pairings from each, the combined probability of drawing DZ twins that are concordant on P_2 is 0.2595. By similar calculations, the likelihood of two zygotes drawn from the P_1-capable matings actually being concordant for P_1 is 0.6699.

From the standpoint of determining zygosity for a set of twins who are concordant on the phenotype in question (P_1 or P_2), these values represent the probability of drawing two matching zygotes from the matings that can produce the reference phenotype. Consequently, they are essential for computing the appropriate DZ values.

The calculations have been performed for all phenotypes in the major bloodgroups, and the results are summarized in Table A-4. The first column gives the likelihood of obtaining one zygote with the reference phenotype, and the second column gives the likelihood of obtaining two zygotes matched on the reference phenotype, based on the complete population values. The latter is equivalent to the proportion of DZ pairs in the population that are expected to be concordant for the reference phenotype.

The third column represents the proportion of matings in the population that are capable of producing the reference phenotype. As described above, this value is used to adjust the one-zygote and two-zygote probabilities, so that they reflect the likelihood of drawing the reference phenotype from the capable matings. The adjusted values are shown in the final two columns of Table A-4 (also previously in text Table 3), and they are to be used in calculating the two composite p-values that enter into the final zygosity equation.

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TABLE A-4. Probabilities of Obtaining One Zygote and Two Concordant Zygotes for All Phenotypes in the Eight Major Bloodgroups

Blood group	Phenotype	Population values		Proportion of capable matings	From capable matings	
		One zygote	Two concordant zygotes		One zygote	Two concordant zygotes
ABO	O	0.475	0.338	0.816	0.582	0.415
	A_1	0.292	0.180	0.532	0.548	0.338
	A_2	0.084	0.040	0.199	0.420	0.202
	B	0.114	0.057	0.261	0.435	0.217
	A_1B	0.027	0.009	0.095	0.287	0.092
	A_2B	0.009	0.003	0.034	0.269	0.077
Rhesus	cde/cde	0.159	0.077	0.406	0.391	0.191
	{CDe/cde, CDe/cDe}	0.344	0.166	0.727	0.472	0.228
	{CDe/CDe, CDe/Cde}	0.146	0.066	0.371	0.395	0.177
	CDe/cDE	0.106	0.042	0.297	0.356	0.140
	{cDE/cde, cDE/cDe}	0.134	0.052	0.339	0.396	0.152
	cDE/cDE	0.021	0.007	0.068	0.304	0.096
	cDe/cde	0.055	0.018	0.158	0.351	0.113
	Cde/cde	0.012	0.003	0.030	0.411	0.112
	cdE/cde	0.004	0.001	0.004	0.791	0.123
Rare genotypes		0.019	0.003	Not calculated	–	–
MNSs	MS/MS	0.044	0.019	0.120	0.365	0.158
	MS/Ms	0.130	0.056	0.370	0.353	0.150
	Ms/Ms	0.101	0.043	0.291	0.348	0.148
	MS/NS	0.036	0.013	0.114	0.311	0.112
	{MS/Ns, Ms/NS}	0.210	0.091	0.551	0.381	0.166
	Ms/Ns	0.246	0.121	0.598	0.411	0.202
	NS/NS	0.008	0.002	0.028	0.280	0.087
	NS/Ns	0.067	0.026	0.200	0.335	0.132
	Ns/Ns	0.144	0.070	0.369	0.390	0.191
P	P+	0.736	0.623	0.930	0.791	0.670
	P–	0.264	0.151	0.583	0.453	0.259
Kell	K+	0.088	0.047	0.168	0.523	0.282
	K–	0.912	0.872	0.996	0.916	0.875
Kidd	Jk^a+	0.753	0.645	0.939	0.802	0.686
	$Jk^a–$	0.247	0.138	0.558	0.443	0.248
Duffy	Fy^a+	0.624	0.493	0.859	0.727	0.574
	$Fy^a–$	0.376	0.245	0.723	0.520	0.338
Lewis	Le^a+	0.229	0.125	0.531	0.432	0.236
	$Le^a–$	0.771	0.667	0.947	0.813	0.704

Note: All calculations carried to five digits before final figure rounded to three digits.

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